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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/717,993	11/20/2003	Chi Li Liu	2027.631000	7643
23720	7590	09/13/2006	EXAMINER	
WILLIAMS, MORGAN & AMERSON 10333 RICHMOND, SUITE 1100 HOUSTON, TX 77042			MEAH, MOHAMMAD Y	
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 09/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<p align="center">Office Action Summary</p>	<p>Application No.</p> <p align="center">10/717,993</p>	<p>Applicant(s)</p> <p align="center">LIU ET AL.</p>	
	<p>Examiner</p> <p align="center">Mohammad Meah</p>	<p>Art Unit</p> <p align="center">1652</p>	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 June 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-23 and 102 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-23 and 102 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>10/5/08, 3/5/04, 12/12/05</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-128 are pending. In response to the election/restriction-office action of date 06/13/2006 of this application, the applicant, on date 06/21/2006 elected without traverse Group I (claims 1-23 and 102) for examination.

Election/Restriction

During preliminary amendment of this application, the applicant, on date 06/21/2006 elected without traverse Group I (claims 1-23 and 102) drawn to method of producing lactic acid using cultured yeast cell for examination. Groups II-IV (claims 24-101 and 103-128) of election/restriction-office action of date 06/13/2006 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected Groups.

Claim Rejections

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-23 and 102 are rejected under U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor at the time the application was filed, had possession of the claimed invention.

Claim 1 line 3 – recitation of “ when cultured in a culture medium”- makes the claim indefinite as it is unclear which medium it referred to any or the first cultured medium previously defined?

Claim 1 line 3 –recitation of “essentially no ethanol” makes the claim unclear as it is unclear if “essentially no ethanol” means no ethanol at all or some minimal ethanol present.

Claim 1 and 102 – in recitation of “wherein a protein resulting from the expression” makes the claim indefinite as it is unclear what is being expressed. Is it meant to be “ wherein a protein resulting from expression of the exogenous LDH gene?”

Claim 8- The recitation of “ essentially the same minimal medium” make the claim unclear because 1.) claim 1 does not recite a “minimal media” as the 1st culture media and 2nd) it is unclear what meaning of “essentially” the same is – i.e what difference are allowed between the same and essentially same. .

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 1-10, 12-20, 22-23 and 102 are rejected under U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor at the time the application was filed, had possession of the claimed invention.

Claims 1-10, 12-23 and 102 are directed to methods of producing lactic acid comprising using any acid- tolerant (AT) yeast expressing with any exogenous Lactose dehydrogenase (LDH) gene from any source. While claims 9-10 are directed to methods of producing lactic acid comprising using acid- tolerant (AT) yeast of *Saccharomyces or candida*, *Kluyveromyces* types expressing with any exogenous Lactose dehydrogenase (LDH) gene. The specification teaches method of preparation of lactic acid using a few modified AT yeast strain expressing with few exogenous Lactose dehydrogenase (LDH) gene (*pdh1*, *pdh5*, etc), which do not represent all AT yeast strains recited in the instant claims. Specification neither teach the structures of all LDH genes nor teach how all AT yeast strain will be modified with all LDH genes. Moreover, the specification fails to describe any other representative species of AT yeast strain by any identifying characteristics or properties other than the acid tolerant LDH activity. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 1-10, 12-23 and 102 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of producing lactic acid

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comprising using acid- tolerant (AT) yeast strain of NRRL-Y-30696, NRRL-Y-30697 or NRRL-Y-30698 expressing an exogenous Lactose dehydrogenase (LDH) gene from *Lactobacillus plantarum* in plasmid YEpLDH, does not reasonably provide enablement for methods of producing lactic acid comprising using any acid- tolerant (AT) yeast strain expressing any exogenous Lactose dehydrogenase (LDH) gene. The claims broadly recite the methods of producing lactic acid comprising using any acid- tolerant (AT) yeast strain expressing any exogenous Lactose dehydrogenase (LDH) gene. The specification fails to describe how any acid- tolerant (AT) yeast strain expressing any exogenous Lactose dehydrogenase (LDH) gene can produce lactic acid and fails to teach how to make nucleic acids encoding any LDH as needed to practice the scope of the claimed methods.

Claims 1-9, 12-23 and 102 are so broad as to include methods of producing lactic acid comprising using any acid- tolerant (AT) yeast strain expressing any exogenous Lactose dehydrogenase (LDH) gene, while claim 10 is so broad as to include methods of producing lactic acid comprising using acid- tolerant (AT) yeast of *S. cerevisiae* strain expressing any exogenous Lactose dehydrogenase (LDH) gene and claim 21 is so broad as to include methods of producing lactic acid comprising using any acid- tolerant (AT) yeast strain expressing the exogenous Lactose dehydrogenase (LDH) gene of *L. plantarum*. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number methods of producing lactic acid comprising using any acid- tolerant (AT) yeast strain expressing any exogenous Lactose dehydrogenase (LDH)

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gene broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of few LDH genes such as gene in plasmid YEpLDH. While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass methods of producing lactic acid comprising using any acid- tolerant (AT) yeast strain expressing any exogenous Lactose dehydrogenase (LDH) gene broadly encompassed by the claims because the specification does not establish: (A) regions of the gene structure which may be modified without effecting lactate dehydrogenase activity and expression of any AT yeast strain with such LDH gene; (B) the general

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tolerance of lactate dehydrogenase gene as well as yeast strain to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any lactate dehydrogenase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any method of producing lactic acid comprising using any acid- tolerant (AT) yeast strain expressing any exogenous Lactose dehydrogenase (LDH) gene broadly encompassed by the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of LDH genes, having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

CLAIM Rejection - 35 U.S.C 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1-10, 12-23, 102 are rejected under 35 U.S.C. 102(b) as being anticipated by Hause et al. (US 2003/0228671). Hause et al. teach various recombinant yeasts (*Saccharomyces*, *Kluyvermyces*, etc) which produce high yield of lactic acid (95 gm/ 100 gram of glucose) at low pH (bellow ~2.3) in a culture medium containing at least among others glucose and one nitrogen source, wherein said yeast expresses (through integration to yeast chromosome or through plasmid) various exogenous LDH genes including from *Lactobacillus plantarum*. They also teach the production and isolation of lactic acid at high yield (i.e. 95% or 95gm/ gm of sugar used) without producing any pyruvate at low pH (bellow ~ 2.3) using nitrogen as nutrient and carbohydrate (glucose, etc) as only carbon source.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mohammad Meah whose telephone number is 571-272-1261. The examiner can normally be reached on 8:30-5PM.

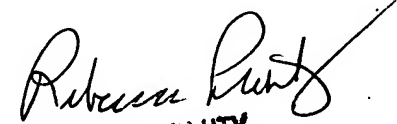
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status

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